REMARKS

On entry of this amendment, claim 6 is cancelled. Accordingly, claims 1-5 and 7-56 are currently pending in this application. Claims 23-31 are withdrawn from consideration as allegedly drawn to unelected embodiments, and claims 1-5, 7-22, and 32-56 are under consideration.

Independent claims 1, 5, and 19 are currently amended. Support for these amendments can be found in the specification and claims as originally filed, for example, at paragraphs [050] and [051] of the specification as filed, and the Examples. Accordingly, the claims have written description support.

FORMAL MATTERS

A. Withdrawn Objections and Rejections

Applicant acknowledges, with appreciation, that the Office has withdrawn the following rejections:

- The rejection of claims 1-5 and 7-22 as allegedly indefinite; and
- The rejection of claims 5, 6, and 19-22 as allegedly anticipated by Frengen in view of Chandler.

See Office Action at 2 (indicating that rejections not reiterated are withdrawn).

B. Information Disclosure Statement

Applicant thanks the Examiner for providing an initialed copy of the Form SB-08 that was filed April 3, 2002, indicating that the Office has considered all of the documents listed on that form.

REJECTIONS UNDER 35 U.S.C. § 112, ¶ 2

Claim 6 stands rejected as allegedly indefinite with respect to the terms "shortly" and "at the latest." Office Action at 2-3. Applicant respectfully disagrees and traverses. However, solely to facilitate prosecution and without acquiescing to the Office's rationale, claim 6 is cancelled herein in view of the amendment of claim 5, rendering this rejection moot. Applicant therefore requests its withdrawal.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 1-4 and 7-15 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,739,042 to Frengen et al. ("Frengen") in view of U.S. Patent No. 5,981,180 to Chandler et al. ("Chandler"). Office Action at 3. Frengen is cited by the Office for allegedly teaching a method involving incubating a sample with two independently determinable solid supported binding partners and a labeled ligand. The Office takes the position that these read on the analyte-A specific binding partners R1, R2, and R3 of claim 1. *Id.* at 3. The Office further alleges that Frengen teaches using "a substantial excess of the second form of solid-supported binding member (R3)." *Id.* at 10. The Office also alleges that Frengen teaches the use of flow cytometry and that Chandler establishes that flow cytometry inherently involves detecting particles at different time intervals. *Id.* at 4.

Applicant respectfully disagrees and traverses. Applicant previously argued that Frengen does not provide guidance regarding the selection of analyte binding partners based on saturation of their analyte binding sites, while the instant claims recite that "saturation of analyte A-binding sites of the binding partner R2 requires a) a higher analyte A concentration, b) a longer incubation, or c) a higher analyte A concentration

and a longer incubation, than does saturation of analyte A-binding sites of the binding partner R3." Furthermore, Applicant argued that Frengen teaches determining measurement signals at the same time, but the instant claims recite "determining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 and time T2 are different." In particular, in Frengen's flow cytometry method, light scattering and fluorescence signals associated with individual particles are detected simultaneously.

However, the Office alleges that Frengen teaches a substantial excess of the second form of solid-supported binding member, which allegedly reads on R3, that the first form of binding partner, which allegedly reads on R2, is supplied in a low amount, and that the member corresponding to R2 requires a longer time than R3 for saturation, for reasons stated in Frengen. Office Action at 10-11. The Office further alleges that Chandler establishes that Frengen teaches flow cytometry methods in which measurements are made of multiple particles and that these measurements do not occur simultaneously, thereby meeting the above limitation. *Id.* at 11.

Solely to facilitate prosecution and without acquiescing to the Office's rationale, independent claim 1 is currently amended to further distinguish it from the cited art. The other claims to which this rejection applies, claims 2-4 and 7-15, all depend directly or indirectly from claim 1. Claim 1 as amended recites in step (iii) either "determining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 <u>is earlier than time T2, time T2 is after addition of label L2, and time T1 occurs before 30% of time from addition of label L2 to time T2 has elapsed</u>; or determining an L1-

dependent measurement signal using a first measurement method and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal using a second measurement method, wherein the first and second measurement methods are different." Applicant respectfully submits that Frengen does not meet either of these limitations.

"A claim is anticipated only if *each and every element* as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987)) (emphasis added). Further, a rejection under Section 102 is proper only when the claimed subject matter is *identically* described or disclosed in the prior art. *In re Arkley*, 455 F.2d 586, 587, 172 U.S.P.Q. 524, 526 (C.C.P.A. 1972) (emphasis added). The identical invention must be described in as complete detail as is contained in, and must be arranged as required by, the claim. M.P.E.P. § 2131.

Frengen does not teach a method comprising "determining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 is earlier than time T2, time T2 is after addition of label L2, and time T1 occurs before 30% of time from addition of label L2 to time T2 has elapsed" that also meets all other limitations of the claims. The methods of Frengen do not teach performing an assay in which the above limitation is met, at least because in the methods of Frengen, times T1 and T2 are at least approximately the same. In Frengen, both the L1 dependent signal and the L2

dependent signal are measured flow cytometrically as a mixture of L1- and L2-bearing particles flow through an Examination chamber.

Frengen teaches that "the process of the invention avoids any need to allow the first form of solid supported binding partner to reach equilibrium with the analyte, a process which may take e.g. up to 24 hours . . . . Th[u]s a substantial benefit of the method of the invention is that it permits the overall assay to be completed in times which may be as short as e.g. 1 to 2 hours." *Id.* at col. 5 lines 17-20 and 23-26. Due to the possible lack of equilibrium, meaning that the reaction is ongoing, one of ordinary skill would understand that the measurement of the particles should be completed quickly, in order to minimize error that would result from particles measured near the end of the measurement period being from a more distinct population (one closer to equilibrium) from the particles measured near the beginning of the measurement period. Furthermore, flow cytometry is capable of rapid measurements; see, e.g., Chandler at col. 10 lines 4-6 ("For example, the 'FACSCAN' flow cytometer can process, or measure, approximately 2,000 beads per second").

Thus, because Frengen teaches measurement of a mixture of the L1- and L2-bearing particles that is not at equilibrium, and encourages rapid measurement of which flow cytometers are fully capable, there is no teaching in Frengen that the times T1 and T2 be separated such that "T1 occurs before 30% of time from addition of label L2 to time T2 has elapsed."

Regarding Chandler, Applicant respectfully submits that Chandler cannot establish that Frengen inherently meets the above-quoted limitation because Chandler does not provide information about the timing of label L2 addition in Frengen's methods,

and therefore cannot establish that "time T1 occurs before 30% of time from addition of label L2 to time T2 has elapsed."

Alternatively, the method of claim 1 can involve "determining an L1-dependent measurement signal using a first measurement method and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal using a second measurement method, wherein the first and second measurement methods are different." Frengen does not meet this limitation either. Both the L1-dependent measurement signal and the L2-dependent measurement signal in Frengen are determined using flow cytometry. Chandler, cited by the Examiner as allegedly establishing inherent properties of flow cytometry, has no relevance to whether Frengen meets this limitation.

Thus, Frengen does not describe a method comprising "determining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 is earlier than time T2, time T2 is after addition of label L2, and time T1 occurs before 30% of time from addition of label L2 to time T2 has elapsed; or determining an L1-dependent measurement signal using a first measurement method and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal using a second measurement method, wherein the first and second measurement methods are different" that also meets all other limitations of the claims, and Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 102(b).

REJECTIONS UNDER 35 U.S.C. § 103

A. Claims 5, 6, 19-22, 32-42, and 46-53

Claims 5, 6, 19-22, 32-42, and 46-53 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Bayer et al., "The Avidin-Biotin System," *Immunoassay* pp. 237-267 (1996) ("Bayer"). Office Action at 5-6. Bayer is cited for allegedly teaching the use of avidin-biotin binding in immunoassays, including to mediate between a primary antibody and a label. *Id.* at 6.

Applicant respectfully disagrees and traverses. However, like claim 1, independent claims 5 and 19 are currently amended to recite that their methods comprise "determining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 is earlier than time T2, time T2 is after addition of label L2, and time T1 occurs before 30% of time from addition of label L2 to time T2 has elapsed; or determining an L1-dependent measurement signal using a first measurement method and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal using a second measurement method, wherein the first and second measurement methods are different." As discussed above, these limitations are not taught by Frengen.

Applicant respectfully submits that Bayer does not remedy this deficiency, because it does not teach or suggest methods comprising "determining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 is earlier than time T2, time T2 is after addition of label L2, and time T1 occurs before 30% of

time from addition of label L2 to time T2 has elapsed; or determining an L1-dependent measurement signal using a first measurement method and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal using a second measurement method, wherein the first and second measurement methods are different." Thus, the claims are not obvious over Frengen in view of Bayer, and Applicant respectfully requests withdrawal of this rejection.

B. Claims 16 and 17

Claims 16 and 17 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Buranda T. et al., "Peptides, Antibodies, and FRET on Beads in Flow Cytometry: A Model System Using Fluoresceinated and Biotinylated β-Endorphin," Cytometry, 37:21-31 (1999) ("Buranda"). Office Action at 7. Buranda is cited for allegedly teaching the use of fluorescence resonance energy transfer in flow cytometric determinations of binding constants. *Id.*

Applicant respectfully disagrees and traverses. However, claims 16 and 17 depend from claim 1 directly or indirectly, and claim 1 has been amended as discussed above to further distinguish it from Frengen. Furthermore, Applicant respectfully submits that Buranda does not remedy the deficiency of Frengen, because Buranda does not teach or suggest methods comprising "determining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 is earlier than time T2, time T2 is after addition of label L2, and time T1 occurs before 30% of time from addition of label L2 to time T2 has elapsed; or determining an L1-dependent measurement signal using a first measurement method and an L2-dependent

measurement signal or an L1 plus L2-dependent measurement signal using a second measurement method, wherein the first and second measurement methods are different." Thus, the claims are not obvious over Frengen in view of Buranda, and Applicant respectfully requests withdrawal of this rejection.

C. Claims 16 and 18

Claims 16 and 18 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Ullman E.F.. et al., "Luminescent Oxygen Channeling Immunoassay: Measurement of Particle Binding Kinetics by Chemiluminescence," PNAS, 91:5426-30 (1994) ("Ullman"). Office Action at 7-8. Ullman is cited for allegedly teaching particles comprising photosensitizers and chemiluminescent compounds utilized in luminescent immunoassays. *Id.*

Applicant respectfully disagrees and traverses. However, claims 16 and 18 depend from claim 1 directly or indirectly, and claim 1 has been amended as discussed above to further distinguish it from Frengen. Furthermore, Applicant respectfully submits that Ullman does not remedy the deficiency of Frengen, because Ullman does not teach or suggest methods comprising "determining an L1-dependent measurement signal at time T1 and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal at time T2, wherein time T1 is earlier than time T2, time T2 is after addition of label L2, and time T1 occurs before 30% of time from addition of label L2 to time T2 has elapsed; or determining an L1-dependent measurement signal using a first measurement method and an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal using a second measurement method, wherein the first and second measurement methods are different." Thus, the claims are not obvious

over Frengen in view of Ullman, and Applicant respectfully requests withdrawal of this rejection.

D. Claims 43, 44, 54, and 55

Claims 43, 44, 54, and 55 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Bayer and Buranda. Office Action at 8.

Applicant respectfully disagrees and traverses. However, these claims depend from claims 5 or 19 directly or indirectly, and claims 5 and 19 have been amended as discussed above to further distinguish them from Frengen. Furthermore, Applicant respectfully submits that, as discussed above, Bayer and Buranda do not remedy the deficiency of Frengen. Thus, the claims are not obvious over Frengen in view of Bayer and Buranda, and Applicant respectfully requests withdrawal of this rejection.

E. Claims 45 and 56

Claims 45 and 56 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Frengen in view of Bayer, Buranda, and Ullman. Office Action at 9.

Applicant respectfully disagrees and traverses. However, claims 45 and 56 depend indirectly from claims 5 and 19, respectively, which have been amended as discussed above to further distinguish them from Frengen. Furthermore, Applicant respectfully submits that, as discussed above, Bayer, Buranda, and Ullman do not remedy the deficiency of Frengen. Thus, the claims are not obvious over Frengen in view of Bayer, Buranda, and Ullman, and Applicant respectfully requests withdrawal of this rejection.

CONCLUSION

Applicant respectfully requests that this Amendment and Reply under 37 C.F.R. § 1.116 be entered by the Examiner, placing the claims in condition for allowance. Applicant respectfully points out that the final action by the Examiner presented some new arguments as to the application of the art against Applicant's invention. It is respectfully submitted that the entering of the Amendment would allow the Applicant to reply to the final rejections and place the application in condition for allowance.

Applicant also submits that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicant submits that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicant therefore requests the entry of this Amendment, the Examiner's reconsideration of the application, and the timely allowance of the pending claims. If the Examiner believes that a telephone conversation would help to resolve any remaining issues, he is respectfully invited to contact the undersigned.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

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Dated: May 14, 2010

By: _____

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